Ultrasonic Detection of *In Vivo* Cells

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Abstract

A current problem in medicine and specifically breast cancer is the detection of microscopic cancer in surgical margins to ensure all of the cancer has been removed. Current methods rely on extensive pathology work that may take several days to complete. For breast cancer patients, positive findings for cancer in surgical margins require follow-up surgery to remove more tissue. Up to 50% of patients undergoing breast conservation surgery (lumpectomy) require additional surgery. A preferable method would be *in vivo* microscopic detection for use during surgery. Such methods would reduce the risks, costs, and patient suffering that accompany follow-up operations.

Ultrasound is a promising *in vivo* detection method due to its low cost, portability, and ability to detect tissue changes arising from cancer. Recent simulations modeling very high frequency (VHF) ultrasonic wave reflections show differences between the reflection signals of a normal breast cell monolayer and a tumor cell monolayer. Experimental measurements of two-dimensional (2D) tissue cultures and control samples support that a single layer of cells can be detected using this method. Simulations of more complex, three-dimensional (3D) tissue structures are ongoing, and future plans include the testing of surgical specimens from breast cancer patients.

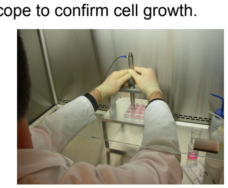
Methods

Computer Simulation Models Used to Simulate Ultrasonic Scattering

- Modeling of cells as spheres containing spherical nuclei [1,2].
- Three different cell types were distinguished by characteristic properties: epithelial, malignant and adipose.
- Development and analysis of different configurations of breast tissue structures.

Experimental Verification

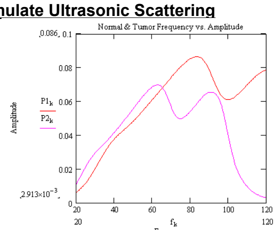
- Two types of cell monolayers were tested: malignant breast and normal breast cells.
- Took human operated measurements every day for four days and once more on day nine.
- Pictures taken every day with microscope to confirm cell growth.



Results

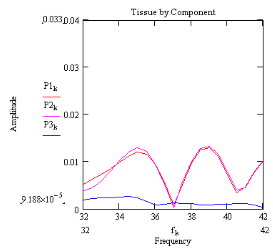
Computer Simulation Models Used to Simulate Ultrasonic Scattering

- Results on the right show amplitude versus frequency for normal cell monolayer (red) and malignant cell monolayer (magenta). Data is not identical for the monolayers.



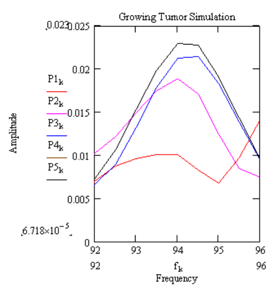
Results

- Results from three dimensional tissue model. Adipose and epithelial cells were simulated alone and then together.

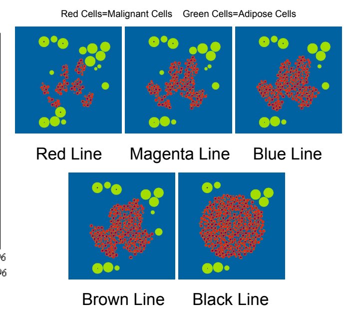


- Red shows epithelial and adipose together results. Magenta is epithelial only. Blue is adipose only.

- Results from three dimensional tissue model of a tumor growing in breast tissue. Each line shows data from a different stage of development.

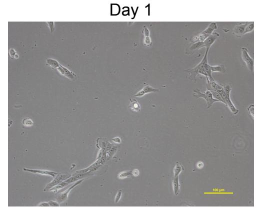


Note: Brown and black are overlapping.

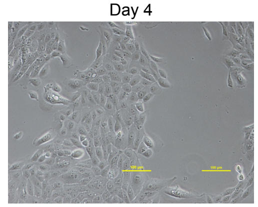


Experimental Verification

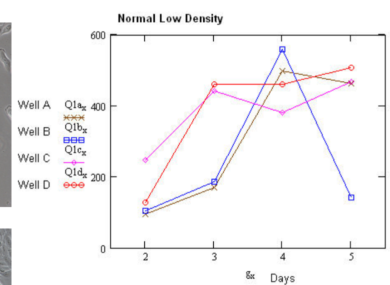
Day 1



Day 4



Photos contributed by collaborating researcher Hemang Patel.



Note: Day 5=Day 9

- On the left are two photos that visually confirm growth in a normal tissue sample.
- Above are ultrasonic amplitudes measured during growth curve experiments for normal breast cell cultures.

Discussion

Computer Simulation Models Used to Simulate Ultrasonic Scattering

- Results from the monolayer simulations presented show it is possible to distinguish between structures that are similar in dimension but different in composition.
- The component simulations show that there are frequencies bands in the spectra at which the received ultrasonic amplitudes are more sensitive to different structures.
- Three dimensional tissue simulations show that there are frequencies that are conducive to detecting the growth of microscopic breast tumors.

Experimental Verification

- The ultrasonic data obtained suggest that a growing microscopic layer of epithelial cells can be detected using ultrasonic waves.
- More data and refinement of detection methods are needed to reduce variability in the data and experimental parameters.

Future Research

Computer Simulation Models

- Further investigation into the effects of epithelial and adipose cluster arrangements and orientations on ultrasonic scattering.
- Investigation of the feasibility of the detection of cancer within epithelial ducts.

Experimental Verification

- Plans to continue tests with cell monolayers using a fixed equipment setup with continuous ultrasonic monitoring to eliminate operator error.
- Continued collaboration to create three dimensional tissue samples for experimental verification of more complex tissue models.
- Tests planned to use human surgical margin samples at the Huntsman Cancer Institute to utilize ultrasonic detection methods on actual tissue specimens.

Conclusions

- Computer simulations suggest that microscopic characteristics associated with the spread of breast cancer can be detected efficiently with ultrasonic methods.
- Initial experimental results show that ultrasonic methods can detect the growth of a single, microscopic layer of breast epithelial cells.
- These results give hope for the possibility that the detection of microscopic cancers in surgical margins is feasible.

References

1. T. E. Doyle, K. H. Warnick, and B. L Carruth, "Histology-based simulations for the ultrasonic detection of microscopic cancer in vivo," Journal of the Acoustical Society of America 122 (6), EL210-EL216 (2007).

2. T. E. Doyle, A. T. Tew, K. H. Warnick, and B. L. Carruth, "Simulation of elastic wave scattering in cells and tissues at the microscopic level," Journal of the Acoustical Society of America 125 (3), 1751-1767 (2009).

Acknowledgements

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